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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,850	03/30/2001	Trey E. Ideker	P-IS 4588	7007

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[REDACTED] EXAMINER

ZEMAN, MARY K

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1631

DATE MAILED: 05/21/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/823,850	IDEKER ET AL.
	Examiner	Art Unit
	Mary K Zeman	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
 - 2a) This action is FINAL. 2b) This action is non-final.
 - 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.
- Disposition of Claims**
- 4) Claim(s) 1-85 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 - 5) Claim(s) _____ is/are allowed.
 - 6) Claim(s) 1-85 is/are rejected.
 - 7) Claim(s) _____ is/are objected to.
 - 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 30 March 2001 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-85 are pending in this application.

Priority

Priority to two separate provisional applications is acknowledged.

Information Disclosure Statement

The IDS filed 12/27/01 has been entered and considered. An initialed copy of the form PTO-1449 is included with this action.

Drawings

The drawings are objected to because they contain shading which obscures detail (Figures 1 and 3), as well as handwritten characters that are difficult to read (Figure 1). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of determining true or relative signals of analytes on microarrays, does not reasonably provide enablement for methods of determining true or relative signals in any situation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a

determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must use the disclosed method steps and algorithms to determine the true signal of an analyte in a sample, or relative levels of analytes in one or more samples. For the reasons discussed below, there would be undue experimentation required to practice the claimed invention.

b) The specification provides guidance for using the disclosed methods to determine the levels of analytes bound to microarrays on pages 19-39. The entirety of the specification is directed to the use of the methods for measuring analytes bound to a microarray or other solid surface. The specification does not set forth how to use the various algorithms and steps to test the signals in other media such as liquid or gas samples.

c) The specification provides working examples of the use of claimed methods on microarray based data in examples I and II. No working examples are present wherein the samples are not microarray based.

d) The invention is drawn to methods of determining the true signal of an analyte in a sample, or relative levels of analytes in one or more samples, wherein the sample is not limited to microarrays, and includes liquid samples, tissue samples, solids, vapor samples etc..

e) The nature of the sample can affect the data generated therefrom. Generally, particular error functions, or constants, or parameter estimations are used that are particular to a given situation- the measurement of an analyte in a liquid generates differing types of data than the measurement of a solid, or the presence of an analyte in a gas, or on an array. The specification does not address any of these issues in regards to the claimed methods..

f) The skill of those in the art of molecular biology is high.

g) The prior art predicts that one needs to account for the type of sample being used to properly estimate signal data. Variables that assess temperature, pressure, volume, density etc. have differing relevance depending upon the data used.

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h) The claims are broad because they are drawn to methods of determining the true signal of an analyte in a sample, or relative levels of analytes in one or more samples, wherein the sample is not limited to microarrays, and includes liquid samples, tissue samples, solids, vapor samples etc..

The skilled practitioner would first turn to the instant specification for guidance to practice methods of determining the true signal of an analyte in a sample, or relative levels of analytes in one or more samples. However, the instant specification does not provide specific guidance to practice embodiments which are not microarray based. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that one must generate a way to account for the type of sample being used. Finally, said practitioner would turn to trial and error experimentation to determine such factors. Such represents undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the steps of the method do not result in the determination of a true signal of an analyte. The steps of the method end with the determination of a mean signal for that analyte. No steps relate the mean signal to a true signal, and no steps set forth the manipulations required to do so. The claims dependent from claim 1 do not remedy this deficiency.

Similarly, each of the independent claims (16, 34, 71, 83 and 85) lack steps that meet the preamble of the method. As such they are all indefinite. The claims dependent thereon do not remedy this deficiency.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-85 are rejected under 35 U.S.C. 102(b) as being anticipated by Stark et al. (USP 5,568,400).

The claims are drawn to methods of determining true or relative levels of one or more analytes in a sample, wherein additive and multiplicative errors and system parameter properties are used to calculate maximum likelihood estimations and probabilities from observed measurements and mean measurements. The errors can comprise differing types of distributions. The methods can further comprise non-linear optimization algorithms.

Stark et al. (USP 5,568,400) discloses methods of detecting analytes wherein measurements of spectral data are obtained from samples. Average and mean data are obtained. Additive and multiplicative error coefficients are calculated. Both linear and non linear multivariate estimation methods to determine necessary corrections to the observed measurements of the sample. Modeling of data can be done by maximum likelihood regressions. The equations of Stark et al. appear to be the same as, or slight rearrangements of those set forth in the instant application. Therefore, this disclosure meets the limitations of the claims.

Claims 1-85 are rejected under 35 U.S.C. 102(a) as being anticipated by Ideker et al. (2000).

Ideker et al. (Journal of Computational Biology Vol. 7 No. 6 pages 805-817 (4/3/00)) discloses Maximum likelihood analysis of microarray data wherein the true or relative analyte signal is obtained. This document has a differing inventive entity from the instant application, and was published within the year prior to the filing date of the instant application. The same methods as those being claimed are disclosed and explained.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The following patents are representative of the art of analyte detection and analysis:

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Modlin et al. 6,503,719

Haaland et al. 6,341,257

Dunn et al. 6,326,160

Braig et al. 6,161,028

Thomas et al. 5,857,462.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

Official fax numbers for this Art Unit are: (703) 308-4242, (703) 872-9306. An *unofficial* fax number, direct to the Examiner is (703) 746 5279. Please call prior to use of this number.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the TC1600 Receptionist whose telephone number is (703) 308-0196.

mkz
5/16/03


MARY K. ZEMAN
PRIMARY EXAMINER
